X-linked Hydrocephalus with Aqueductal Stenosis: L1CAM Gene Deletion/Duplication

Condition Description

Mutation of the L1CAM gene (Xq28) is characterized by hydrocephalus, mental retardation, spasticity of the legs, and adducted thumbs. The phenotypic spectrum L1CAM mutations includes X-linked hydrocephalus with stenosis of the aqueduct of Sylvius (HSAS), MASA syndrome (mental retardation, aphasia (delayed speech), spastic paraplegia (shuffling gait), adducted thumbs), SPG1 (X-linked complicated hereditary spastic paraplegia type 1), and X-linked complicated corpus callosum agenesis. The group of conditions as a whole can be referred to as L1 syndrome.

Hydrocephalus in L1 syndrome may be present prenatally and result in stillbirth or death in early infancy. Males with HSAS are born with severe hydrocephalus and adducted thumbs. Seizures may occur. In less severely affected males, hydrocephalus may be subclinically present and documented only because of developmental delay. Mild-to-moderate ventricular enlargement is compatible with long survival. Mental retardation is usually severe and is independent of shunting procedures in individuals with severe hydrocephalus. In MASA syndrome, mental retardation ranges from mild (IQ of 50-70) to moderate (IQ of 30-50). The degree of intellectual impairment does not necessarily correlate with head size or severity of hydrocephalus; males with severe mental retardation and a normal head circumference have been reported. All phenotypes can be observed in affected individuals in the same family. Females may manifest minor features such as adducted thumbs and/or subnormal intelligence. Rarely do females manifest the complete L1 syndrome phenotype.

X-linked hydrocephalus with stenosis of the aqueduct of Sylvius is the most common genetic form of congenital hydrocephalus, with a prevalence of approximately one in 30,000. This accounts for approximately 5%-10% of males with nonsyndromic congenital hydrocephalus.

While mutation detection rates are unknown, point mutations, partial gene deletions, and partial gene duplications have all been reported. Although uncommon, de novo disease-causing mutations have been reported.

Click here for the GeneTests summary on this condition.

Genes

L1CAM

Indications

This test is indicated for:

- Confirmation of a clinical diagnosis of L1 syndrome in individuals who have tested negative for sequence analysis
- Carrier testing in adult females with a family history of L1 syndrome who have tested negative for sequence analysis

Methodology

DNA isolated from peripheral blood is hybridized to a CGH array to detect deletions and duplications. The targeted CGH array has overlapping probes which cover the entire genomic region. Please note that a “backbone” of probes across the entire genome are included on the array for analytical and quality control purposes. Rarely, off-target copy number variants causative of disease may be identified that may or may not be related to the patient’s phenotype. Only known pathogenic off-target copy number variants will be reported. Off-target copy number variants of unknown clinical significance will not be reported.

Detection

Detection is limited to duplications and deletions. The CGH array will not detect point or intronic mutations. Results of molecular analysis must be interpreted in the context of the patient’s clinical and/or biochemical phenotype.

Specimen Requirements
Submit only 1 of the following specimen types

* Preferred specimen type: Whole Blood

**Type: Whole Blood**

Specimen Requirements:

In EDTA (purple top) tube:
- Infants (2 years): 3-5 ml
- Older Children & Adults: 5-10 ml

Specimen Collection and Shipping: Refrigerate until time of shipment. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Type: Saliva**

Specimen Requirements:

Oragene™ Saliva Collection kit (available through EGL) used according to manufacturer instructions.

Specimen Collection and Shipping: Store sample at room temperature. Ship sample within 5 days of collection at room temperature with overnight delivery.

**Special Instructions**

Submit copies of diagnostic biochemical test results with the sample, if appropriate. Contact the laboratory if further information is needed.

Sequence analysis is required before deletion/duplication analysis by targeted CGH array. If sequencing is performed outside of EGL Genetics, please submit a copy of the sequencing report with the test requisition.

**Related Tests**

- Sequencing analysis of the L1CAM gene is available and is required before deletion/duplication analysis.
- A CGH array-based test for deletion/duplication analysis of 109 different X-linked intellectual disability genes is available.
- Prenatal testing is available to adult females who are confirmed carriers of mutations. Please contact the laboratory genetic counselor to discuss appropriate testing prior to collecting a prenatal specimen.